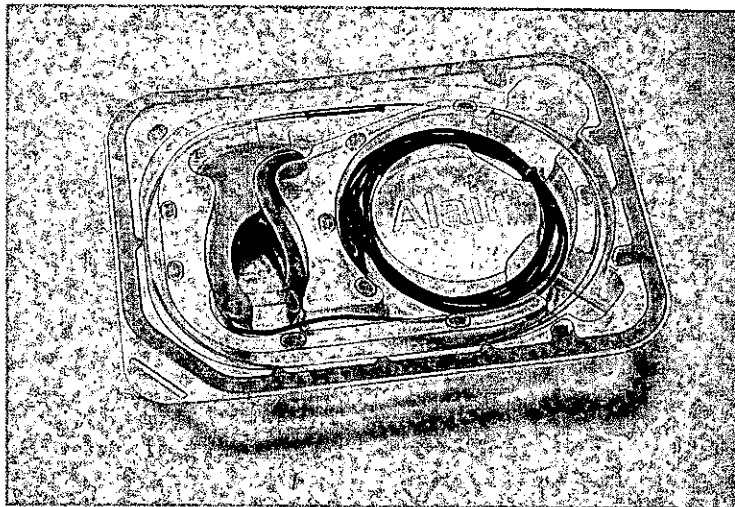


ALAIR®

FOR BRONCHIAL
THERMOPLASTY

INSTRUCTIONS FOR USE

Catheter Model ATS 2-5



Only

United States federal law restricts this device to sale by or on the order of a physician.






The Alair® Catheter must be used by a physician who has training and experience in performing bronchoscopic procedures.

These Instructions for Use (IFU) are specific to the Alair® Catheter Model ATS 2-5. Do not attempt to operate the Alair® Catheter before thoroughly reading this IFU and the Alair® Radiofrequency Controller Model ATS 200 Operator's Manual.

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ALAIR® BRONCHIAL THERMOPLASTY SYSTEM DESCRIPTION

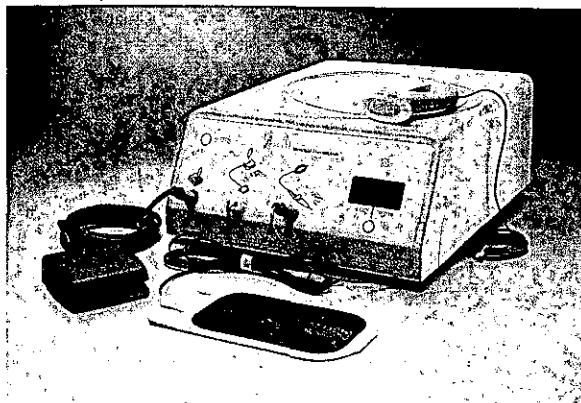


Figure 1: The Alair® Bronchial Thermoplasty System

The Alair® Bronchial Thermoplasty System ("Alair® System"), manufactured by Asthmatx, Inc. ("Asthmatx"), consists of the Alair® Catheter and the Alair® Controller System, as described below:

Alair® Catheter: The Alair® Catheter Model ATS 2-5 ("Catheter") is provided sterile and is a SINGLE-USE ONLY, disposable device. The Catheter delivers energy from the Controller to the desired site in the airway and relays temperature feedback to the Controller. The Alair® Catheter Model ATS 2-5 is designed to be used with the Alair® RF Controller Model ATS 200.

Alair® Controller System

Alair® Radiofrequency (RF) Controller: The Alair® RF Controller Model ATS 200 ("Controller") is designed to provide controlled delivery of RF energy to the Alair® Catheter. Energy from the Controller is delivered to the Catheter through the electrical cable attached to the proximal end of the catheter handle. Actual power delivered is automatically modulated by the Controller based on temperature control algorithms. The Controller delivers low-power, temperature-controlled RF energy to the airway at a predetermined temperature setting for a predetermined time period. The Controller incorporates hardware and software features that limit current, voltage, power, energy, time and temperature during each application of RF energy. The Controller is not intended to come in contact with the patient and therefore is not provided as a sterile device. For information on the installation, use, and other technical specifications, please read the Alair® Radiofrequency Controller Operator's Manual that is supplied with Model ATS 200.

Footswitch: The Controller is supplied with a footswitch that allows the operator to start and stop the delivery of RF energy. The Controller is designed to be used with the compatible footswitch provided by Asthmatx. The footswitch is not intended to come into contact with the patient and therefore is not provided as a sterile device.

Patient Return Electrode: The Controller is designed to be used with a gel-type patient return electrode that is compliant with the applicable portions of IEC 60601-2-2:2006 and/or CE marked. The patient return electrode is used to complete the return path for the electrical current. Use only patient return electrodes indicated for use with adults or patients weighing more than 15 kg (33 lbs). Examples of acceptable patient return electrodes include Valleylab E7506 and ConMed 51-7310. Follow the instructions for use (IFU) packaged with the patient return electrode.

INDICATION FOR USE

The Alair® Bronchial Thermoplasty System is indicated for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists.

BRONCHOSCOPE REQUIREMENTS

The Catheter is designed to be used with high-frequency compatible flexible bronchoscopes that have a minimum 2.0mm working channel, and maximum 5.0mm outer diameter.

MECHANISM OF ACTION

Airway smooth muscle (ASM) consists of muscle tissue within the airway walls in the lung. Contraction of the ASM is a main cause of airway constriction that leads to difficulty in breathing during asthma attacks. Severe asthma patients also experience an increase in ASM mass. This increase, together with inflammation of the airways, combines to thicken airway walls, which decreases the inside diameter of the airways when the ASM contracts. The resulting decrease in airway diameter causes increased resistance to airflow and further contributes to difficulty in breathing during asthma attacks.

The Alair® System is used to deliver thermal energy to the airway wall, to heat the tissue in a controlled manner in order to reduce ASM mass. Bronchial thermoplasty is intended to reduce, debulk, or partially eliminate smooth muscle tissue. In preclinical studies (Danek et al. 2004¹, Brown et al. 2005²), the reduction of ASM has been shown to decrease the ability of the airways to constrict/contract, reduce resistance to airflow and responsiveness of the airway, and increase the resting diameter of the airway.

CONTRAINDICATIONS

Patients with the following conditions should not be treated:

- Presence of a pacemaker, internal defibrillator, or other implantable electronic devices,
- Known sensitivity to medications required to perform bronchoscopy, including lidocaine, atropine, and benzodiazepines,
- Patients previously treated with the Alair® System should not be retreated in the same area(s). No clinical data are available studying the safety and/or effectiveness of repeat treatments.

Patients should not be treated while the following conditions are present:

- Active respiratory infection,
- Asthma exacerbation or changing dose of systemic corticosteroids for asthma (up or down) in the past 14 days,
- Known coagulopathy,
- As with other bronchoscopic procedures, patients should stop taking anticoagulants, antiplatelet agents, aspirin and NSAIDs before the procedure with physician guidance.

¹ Danek CJ, Lombard CM, Dungworth DL, Cox PG, Miller JD, Biggs MJ, Keast TM, Loomas BE, Wizeman WJ, Hogg JC, Leff AR. Reduction in airway hyperresponsiveness to methacholine by the application of RF energy in dogs. J Appl Physiol. 2004, 97(5):1946-53.

² Brown RH, Wizeman W, Danek C, Mitzner W. Effect of bronchial thermoplasty on airway distensibility. Eur Respir J. 2005 Aug;26(2):277-82.

WARNINGS

READ THESE INSTRUCTIONS FOR USE IN CONJUNCTION WITH THE ALAIR® RF CONTROLLER MODEL ATS 200 OPERATOR'S MANUAL BEFORE USING THE ALAIR® BRONCHIAL THERMOPLASTY SYSTEM. FAILURE TO FOLLOW ANY INSTRUCTIONS OR FAILURE TO HEED ANY WARNINGS OR PRECAUTIONS MAY RESULT IN HARM OR INJURY TO PATIENT.

1. Prior to performing the procedure, ensure appropriate training, equipment, medications and staff are in place to handle any potential bronchoscopic, respiratory or anesthesia related emergencies. The Alair® System should only be used in a fully equipped bronchoscopy suite with access to full resuscitation equipment to handle hemoptysis, pneumothorax, and other respiratory complications including acute exacerbation of asthma and respiratory failure requiring intubation.
2. Do not deliver energy if the Catheter's electrode array is in contact with a metal object. This may result in harm or injury to the patient and/or operator.
3. Do not advance the Catheter within the bronchoscope if significant resistance is felt, as this may result in harm or injury to the patient and/or cause damage to the Catheter and/or bronchoscope.
4. Do not advance the Catheter into bronchi in which the Catheter cannot be seen under bronchoscopic vision. Advancing the Catheter beyond this region may cause patient harm or injury such as pneumothorax or pneumomediastinum.
5. Do not reposition the bronchoscope with the Catheter advanced beyond the distal end of the bronchoscope as this may result in patient harm or injury.
6. Use of the Alair® Catheter with a non-Alair® Controller may result in harm or injury to the patient and/or operator, or may result in product malfunction.
7. Do not treat the right middle lobe because of the potential susceptibility of the right middle lobe to transient obstruction as a result of inflammation or edema due to certain anatomical characteristics. The narrow diameter of the lobar bronchus and acute take-off angle may create poor conditions of drainage that may cause patient harm or injury such as atelectasis or difficulty in re-inflation (Right Middle Lobe Syndrome).

PRECAUTIONS

1. The Alair® Catheter is provided sterile and is SINGLE USE ONLY. Do not use the Catheter if the package is opened, torn, or damaged. Use of a Catheter from damaged packaging may result in patient harm or injury. **Do not re-sterilize or reuse** the Catheter, as this may result in patient harm or injury, transmittal of infectious disease or product malfunction.
2. Do not use the Catheter if it comes in contact with a surface that is not aseptic (e.g. floor). This may result in patient infection.
3. Do not use the Catheter if it is damaged or irregular. Use of a damaged or irregular Catheter may result in patient harm or injury.
4. Do not use the Catheter if the marker bands are missing (See Directions for Use, Figure 5).
5. Use care when handling the Catheter to avoid kinking the Catheter shaft.
6. Avoid deflecting the bronchoscope while the electrode array is within the bend of the bronchoscope's working channel as this may result in damage to the Catheter and failure of the Catheter to operate properly.
7. Before inserting or removing the Catheter from the bronchoscope, ensure the electrode array is relaxed. Do not use the Catheter if the electrode array does not expand or relax properly (See Directions for Use, Figure 6 and Figure 7).
8. Before delivering energy, make certain that all electrodes are in contact with the airway wall.

9. Caution should be taken in patients with the following conditions due to a potential increased risk of adverse events that may be associated with the procedure. Patients with these conditions were not studied in the pivotal trial and the safety of Alair® treatment for such patients has not been determined:
- Post-bronchodilator FEV₁ < 65% predicted.
 - Other respiratory diseases including emphysema, vocal cord dysfunction, mechanical upper airway obstruction, cystic fibrosis or uncontrolled obstructive sleep apnea.
 - Use of short acting bronchodilator in excess of 12 puffs per day within 48 hours of bronchoscopy (excluding prophylactic use for exercise).
 - Use of oral corticosteroids in excess of 10 milligrams per day for asthma.
 - Increased risk for adverse events associated with bronchoscopy or anesthesia, such as pregnancy, insulin dependent diabetes, epilepsy or other significant co-morbidities, such as uncontrolled coronary artery disease, acute or chronic renal failure, and uncontrolled hypertension.
 - Intubation for asthma, or ICU admission for asthma within the prior 24 months.
 - Any of the following within the past 12 months:
 - i. 4 or more lower respiratory tract infections (LRTI)
 - ii. 3 or more hospitalizations for respiratory symptoms
 - iii. 4 or more OCS pulses for asthma exacerbation
10. The Alair® System should only be used by clinicians who are experienced in bronchoscopy and have undergone adequate training with the device.
11. The Alair® System should only be used in patients stable enough to undergo bronchoscopy in the judgment of their clinician.
12. Follow local governing ordinances and your institution's biohazard procedures regarding disposal of the Alair® Catheter and patient return electrode.

CLINICAL DATA

Objectives

The pivotal study was a multi-center, randomized, double-blind, sham-controlled study to demonstrate the safety and effectiveness of the Alair® System in a population of subjects with severe asthma.

Effectiveness Endpoints

The primary effectiveness endpoint was the difference between treatment (Alair) and control (Sham) groups in the change in the Asthma Quality of Life Questionnaire (AQLQ) score between baseline and the average of 6-, 9-, and 12-month follow-up visits (integrated AQLQ score). Other endpoints included: rates of severe asthma exacerbations, proportions of patients with severe asthma exacerbations, and days lost from work, school, or other daily activities due to asthma symptoms. In addition, several safety endpoints were considered for effectiveness; these endpoints included rates of asthma (multiple symptoms)* adverse events, Unscheduled Physician Office visits for respiratory symptoms, Emergency Room visits for respiratory symptoms, and Hospitalizations for respiratory symptoms.

* "Asthma (multiple symptoms)" is defined as occurrence or worsening of shortness of breath, wheeze, cough, productive cough, or some combination of these.

Methods

This was a multicenter, randomized (2 Alair, 1 Sham), double-blind, sham-controlled clinical trial comparing the effects of treatment with the Alair® System to a Sham treatment in subjects that were optimized to conventional therapy of inhaled corticosteroids (ICS) and long-acting β_2 -agonists (LABA). All subjects included in the Study were taking ICS ($> 1000\mu\text{g}$ beclomethasone or equivalent per day) and LABA ($\geq 100\mu\text{g}$ salmeterol or equivalent per day), and were still symptomatic.

Subjects in the Alair and Sham groups were administered the Alair® treatment and Sham bronchoscopies, respectively, by an unblinded bronchoscopy team in 3 separate bronchoscopy sessions. Each bronchoscopy session was separated by at least 3 weeks. All bronchoscopy sessions were administered under local anesthesia with sedation. Subjects had follow-up visits with blinded asthma assessment teams at 6-weeks, 12-weeks, 6-months, 9-months, and 12-months after the final bronchoscopy session.

All subjects were prescribed to take 50mg of oral prednisone or prednisolone (or equivalent) each day for 5 days covering the 3 days before the bronchoscopy session, the day of the bronchoscopy session, and the day after the bronchoscopy session (prophylactic indication).

Statistical Plan

Primary and secondary endpoints, as well as adverse events were analyzed using Bayesian statistics. The Posterior Probability of Superiority was calculated for the primary and secondary endpoints, as well as safety outcomes.

Patient Population

Enrollment was limited to patients with severe persistent asthma who were still symptomatic despite being managed on conventional therapy of high dose ICS and LABA. Subjects may have been taking up to 10 milligrams of oral corticosteroids per day. Study subjects were required to meet the following patient selection criteria:

Key Entry Criteria

Inclusion

1. Adult; age 18-65 years.
2. Asthma requiring regular maintenance medication that includes inhaled corticosteroids (greater than 1000 μg beclomethasone per day or equivalent) and long-acting β_2 -agonists (at least 100 μg salmeterol per day or

- equivalent), with or without other asthma medications. Oral corticosteroids at a dosage of up to, but not greater than 10mg per day, or 20 milligrams every other day are acceptable.
3. Asthma Quality of Life Questionnaire Score during the Baseline Phase of 6.25 or less.
 4. Pre-bronchodilator forced expiratory volume in one second $\geq 60\%$ predicted (after patients stabilized on inhaled corticosteroids and long-acting β_2 -agonists during the Baseline Phase).
 5. Non-smoker x 1 year or greater (if former smoker, less than 10 pack years total smoking history).

Exclusion

1. Post-bronchodilator FEV₁ <65% predicted.
2. Three or more hospitalizations for exacerbations of asthma in the previous year; OR a history of life-threatening asthma, defined by past intubations for asthma, or intensive care unit admission for asthma within the prior 24 months.
3. History of recurrent lower respiratory tract infection requiring antibiotics (more than 3 in the past 12-Months).
4. History of recurrent oral steroid use for asthma (4 or more pulses of oral steroids in the past 12-Months).

Demographics

A total of 297 subjects between the ages of 18 and 65 were enrolled and randomized (2 Alair: 1 Sham) in this study. One hundred and ninety (190) received the Alair[®] treatment and 98 received the Sham control treatment (Intent-to-Treat population). The Sham procedure was identical to the Alair[®] procedure except that no energy was delivered through the Catheter.

There were no statistical differences in demographic measures between the Alair and Sham groups. Subject demographics are described in Table 1.

	Alair (n=190)	Sham (n=98)
Age (years) (Mean \pm SD)	41 \pm 12	41 \pm 12
Gender		
Male	81 (43%)	38 (39%)
Female	109 (57%)	60 (61%)
Race/Ethnicity		
Caucasian	151 (80%)	72 (74%)
African American / Black	19 (10%)	15 (15%)
Hispanic	6 (3%)	4 (4%)
Asian	4 (2%)	1 (1%)
Other	10 (5%)	6 (6%)
Height (cm) (Mean \pm SD)	167 \pm 9	167 \pm 10
Weight (kg) (Mean \pm SD)	82 \pm 18	82 \pm 20

Table 1: Subject Demographics (Intent-to-Treat Population)

Effectiveness Results

Effectiveness analyses were performed for both the Intent-to-Treat (ITT) population and Per-Protocol (PP) population. The ITT population consisted of all randomized subjects who have been administered at least one bronchoscopy. The PP population excluded all subjects in the ITT population who met any of the following criteria:

- Have taken any interfering concomitant medications.
- Have undergone other interfering treatments.
- Did not attend one of the 6-, 9-, 12-month visits, with the exception of a discontinuation from the Study due to an adverse event related to Study treatment.
- Had missed one or more bronchoscopy procedures.

Effectiveness Endpoints

Although the clinical study was powered only for the primary effectiveness endpoint (see below), several effectiveness endpoints and safety endpoints that could also be considered effectiveness endpoints demonstrated clinically meaningful differences in favor of the Alair group compared to the Sham group. The effectiveness endpoints were rates of severe asthma exacerbations, proportions of patients with severe asthma exacerbations, and days lost from work, school, or other daily activities due to asthma symptoms. The safety endpoints considered for effectiveness were rates of asthma, emergency room visits for respiratory symptoms, and hospitalization rates for respiratory symptoms.

Steroid Exacerbations^a (Severe Exacerbations Requiring Systemic Corticosteroids) (ITT Population)

During the Post-Treatment Phase, the severe exacerbation rate for the Steroid Exacerbations was 0.48 exacerbations/subject/year in the Alair group and 0.70 exacerbations/subject/year in the Sham group [95% CI (Sham - Alair): -0.031, 0.520]. During the Post-Treatment Phase, the proportion of subjects experiencing Steroid Exacerbations was 26% in the Alair group and 40% in the Sham group [95% CI (Sham - Alair): 2.1%, 25.1%].

Steroid Exacerbation rates (annualized rate) and proportion of patients experiencing Severe Exacerbations for the Post-Treatment Phase are presented graphically in **Figure 2**.

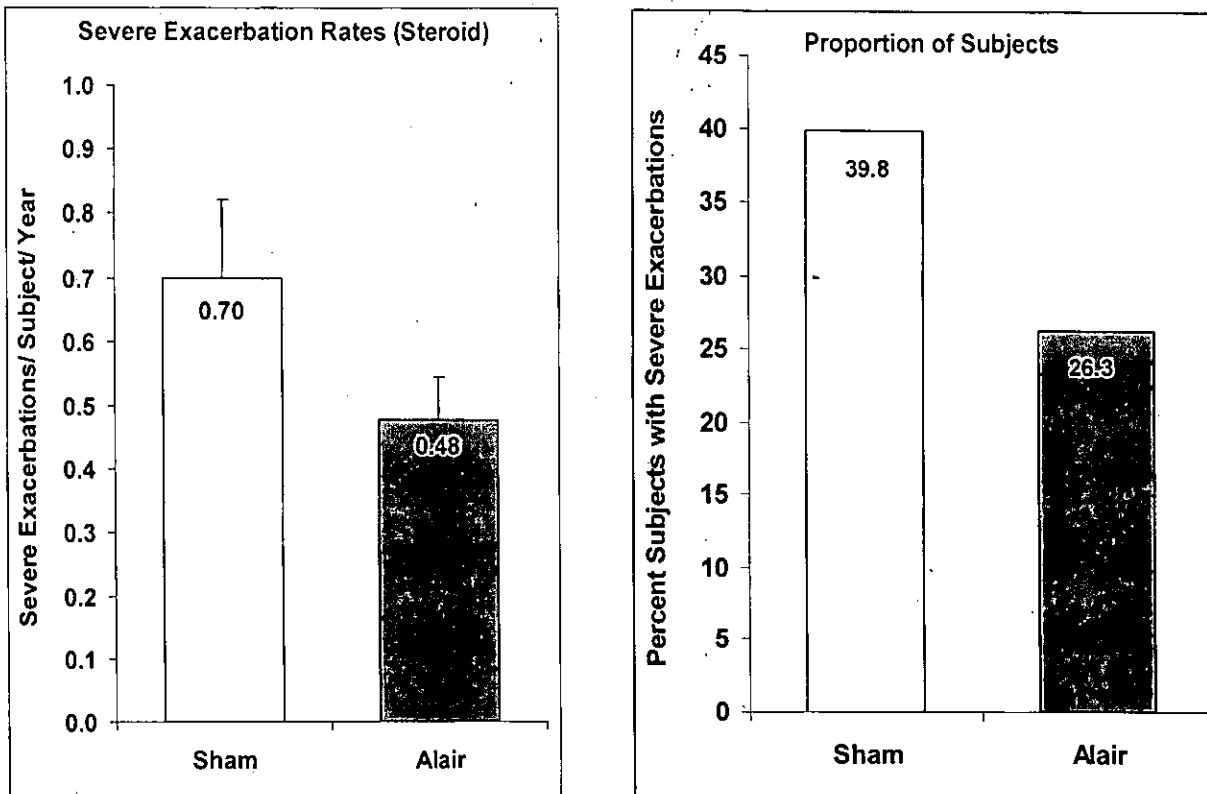


Figure 2: Severe Exacerbations during the Post-Treatment Phase

^a **Steroid Exacerbations** = Exacerbations treated with oral or intravenous corticosteroids, OR a doubling of the baseline inhaled corticosteroid dose for at least 3 days, OR any temporary increase in the dosage of oral corticosteroids for a subject taking maintenance oral corticosteroids at Study entry.

Annualized rates of exacerbations per subject are extrapolated from the 46 week Post-Treatment Phase from 6 weeks after the last bronchoscopy procedure to the 12 month follow-up visit.

Days Lost from Work, School, or Other Daily Activities due to Asthma Symptoms (ITT Population)

During the Post-Treatment Phase, subjects in the Alair group lost an average of 1.3 days/year/subject from work, school, or other daily activities due to asthma symptoms, compared to the Sham group that lost 3.9 days/year/subject (annualized rates per subject are extrapolated from the 46 week Post-Treatment Phase from 6 weeks after the last bronchoscopy procedure to the 12 month follow-up visit) [95% CI (Sham - Alair): 0.425, 6.397].

Safety Endpoints that Demonstrated Effectiveness

Measures such as Emergency Room visits and Hospitalizations for respiratory symptoms are generally considered to be important measures of safety, especially if an intervention results in an increase in the rate of one or more of these events. However, these measures can also be considered important measures of effectiveness if an intervention results in a measurable decrease in the rate of one or more of these events. During longer-term follow-up (> 6 weeks after the last Alair® treatment), there was a reduction in asthma (multiple symptoms) adverse events [95% CI (Sham - Alair): -0.01, 0.001], Emergency Room visits for respiratory symptoms [95% CI (Sham - Alair): 0.11, 0.83], and Hospitalizations for respiratory symptoms (event rate per group) [95% CI (Sham - Alair): 0.025, 0.172, presented graphically in Figure 3.

There was a reduction in the proportion of subjects having asthma (multiple symptoms) adverse events ([95% CI (Sham - Alair): 4.0%, 27.3%]), and in the proportion of subjects having Emergency Room visits for respiratory symptoms in the Alair group (3.7% in the Alair group compared to 15.3% in the Sham group) [95% CI (Sham - Alair): 4.6%, 19.7%].

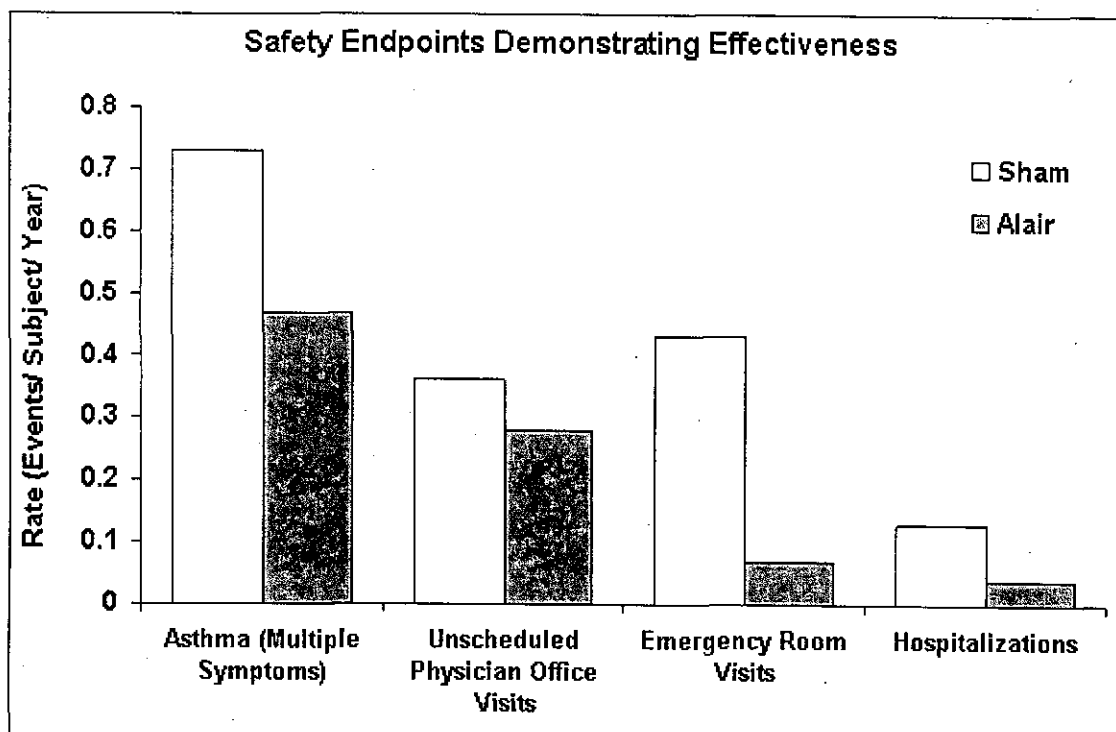


Figure 3: Safety Endpoints demonstrating Effectiveness (ITT Population)

Primary Effectiveness Endpoint – Integrated AQLQ Score

The difference between the Alair and Sham groups in the average change in AQLQ score from Baseline at the 6-, 9-, and 12-month follow-up visits was 0.210 [95% CI (Alair - Sham): -0.025, 0.445]. The pre-specified Posterior Probability of Superiority for the difference between the groups was 96.4%. For the ITT population, the difference between the groups had a Posterior Probability of Superiority of 96.0%, and for the PP population, the difference between the groups had a Posterior Probability of Superiority of 97.9%, demonstrating an improvement in the Asthma Quality of Life in the Alair group compared to Sham.

The results for the change from Baseline of the Integrated AQLQ score for the Intent-to-Treat and Per Protocol populations are summarized in Table 2.

Population	Difference Between Groups in Integrated AQLQ Score (Posterior Mean, 95% CI)	Posterior Probability of Superiority (%)
ITT (Intent-to-Treat) (Alair N=190, Sham N=98)	0.210 (-0.025, 0.445)	96.0
PP (Per Protocol) (Alair N=173, Sham N=95)	0.244 (0.009, 0.478)	97.9

Table 2: Primary Effectiveness Endpoint: Integrated AQLQ Score

ADVERSE EVENTS IN PIVOTAL STUDY

Patient Population

The Alair® System was evaluated in a randomized, double-blind, sham-controlled, multi-center clinical study – the Asthma Intervention Research 2 (AIR2) Trial. A total of 297 subjects with severe persistent asthma who were still symptomatic despite being managed on conventional therapy of high dose ICS and LABA were randomized – 196 subjects in the Alair group and 101 subjects in the Sham group. (See the Clinical Data section for key entry criteria.) The Sham procedure was identical to the Alair® procedure except that no energy was delivered to the Catheter in the sham procedure.

Safety analyses were performed for the Intent-to-Treat (ITT) population (288 subjects) that consisted of all randomized subjects who have been administered at least one bronchoscopy.

Observed Adverse Events

The safety of the Alair® System was assessed by comparing adverse event profiles of the Alair and Sham group subjects. Adverse event profiles are compared for the Treatment Phase (day of first bronchoscopy procedure to 6 weeks after the last bronchoscopy procedure) and Post-Treatment Phase (6 weeks after the last bronchoscopy to the 12 month follow-up visit).

Adverse events (whether considered procedure-related or not procedure-related by the investigator) occurring with \geq 3% incidence that were more common in the Alair group are presented for 288 patients in **Table 3**.

Adverse Event	Treatment ³		Post-treatment ⁴	
	Alair (N=190) %	Sham (N=98) %	Alair (N=187) %	Sham (N=98) %
Average duration of period (days)	84		322	
Ear, Nose, and Throat				
Upper respiratory tract infection	20	11	30	26
Viral Upper respiratory tract infection	4	2	6	7
Nasopharyngitis	5	7	11	5
Acute Sinusitis	3	2	4	8
Rhinitis	2	0	4	6
Lower Respiratory				
Asthma (Multiple Symptoms)	52	39	27	43
Wheezing	15	6	4	3
Dyspnea	11	6	2	1
Bronchitis	4	2	7	5
Chest discomfort	9	10	2	1
Atelectasis	5	0	0	0
Hemoptysis	3	0	0	0
Lower respiratory tract infection	8	2	3	6
Chest pain	14	13	3	1
Neurology				
Anxiety	4	0	1	2
Headaches	14	9	5	3
Gastrointestinal				
Dyspepsia	4	2	2	4
Nausea	3	4	1	1
Non-site specific				
Pyrexia (fever)	4	2	0	1
Influenza	4	2	4	12
Other				
Urinary tract infection	1	1	3	1
Hypertension	3	2	3	3

Table 3: Adverse Events with $\geq 3\%$ incidence (% of subjects) that were more common in the Alair Group

³ Treatment phase represents adverse events reported between the first bronchoscopy and 6-weeks post last bronchoscopy.

⁴ Post-Treatment phase represents adverse events reported between 6-weeks post last bronchoscopy and the 12 month visit.

Adverse events occurring in both the Treatment Phase and Post-Treatment Phase at a rate of <3% and ≥1% (whether considered procedure-related or not procedure-related by the investigator) that were more frequently reported by the Alair group than the Sham group included pneumonia, operative hemorrhage, abnormal breath sounds, bronchial obstruction, acute bronchitis, bronchospasm, lower respiratory tract infection (viral), pulmonary congestion, discolored sputum (blood-tinged sputum), increased upper airway secretion, and viral pharyngitis.

During the Treatment Phase in the AIR2 Trial, there was a transient increase in respiratory adverse events, including asthma (multiple symptoms), upper respiratory tract infection, atelectasis, lower respiratory tract infection, wheezing, hemoptysis, and anxiety in the Alair group compared to the Sham group. There was a lower incidence of throat irritation in the Alair group compared to the Sham group. There were 7 instances of hemoptysis defined as >5.0 mL (1.3% of bronchoscopies) of which 2 occurred on the day of the procedure, 2 occurred within 3 days, 2 occurred at 2 weeks, and one occurred on Day 31 after the procedure. The greatest amount of hemoptysis observed was a cumulative total of 150 mL that occurred over 5 days and was treated with bronchial artery embolization.

During the Treatment Phase (~ 12 weeks period), the rate of Unscheduled Physician Office visits (events / subject / 12 weeks) in the Alair group was 0.230 compared to 0.133 in the Sham group. The rate of hospitalizations for respiratory symptoms (events / subject / 12 weeks) was 0.086 in the Alair group compared to 0.028 in the Sham group. The rate of Emergency Room visits for respiratory symptoms (events / subject / 12 weeks) was 0.062 in the Alair group compared to 0.075 in the Sham group.

During the Post-Treatment Phase in the AIR2 Trial, there was a lower incidence of respiratory symptoms in the Alair group compared to the Sham group, including a 36% reduction in asthma (multiple symptoms) events and proportion of subjects with asthma (multiple symptoms) events. There was also a lower incidence of influenza, and a greater incidence of nasopharyngitis in the Alair group compared to the Sham group.

High Resolution Computed Tomography (HRCT) Results

In the 150 subjects (100 Alair group and 50 Sham group) assigned to HRCT scan examinations, at 1-year, there were no difference in signs of gas trapping or consolidation and there was no evidence of bronchiectasis. A difference was seen in bronchial wall thickening without gas trapping which occurred only in the Sham subjects (4%).

Summary of Clinical Findings

Results from the clinical study which evaluated the effectiveness and safety of the Alair® System in subjects with severe asthma demonstrated that Alair® treatment resulted in clinically significant reductions in severe exacerbations that required systemic steroids, the percent of subjects experiencing the severe exacerbations, the number of Emergency Room visits for respiratory symptoms, the percent of subjects experiencing Emergency Room visits for respiratory symptoms, Hospitalizations for respiratory symptoms, and days lost from school/work/other daily activities due to asthma symptoms. Although bronchial thermoplasty was associated with an increased rate of respiratory adverse events during the Treatment Phase (primarily related to asthma), in the Post-Treatment Phase, a smaller proportion of patients treated with bronchial thermoplasty experienced respiratory adverse events, including asthma (multiple symptoms).

DIRECTIONS FOR USE

Alair® Catheter Inspection and Preparation

1. The Alair® System should only be used by a physician trained in bronchoscopy. These instructions do not explain bronchoscopic procedures.
2. Please read the Operator's Manual for the Alair® RF Controller Model ATS 200 before beginning the procedure.
3. Visually inspect the package for damage before removing the Catheter from the package. Do not use the Catheter if the package is damaged or has been previously opened or torn.
4. Aseptically remove the Catheter from the package tray and inspect for any damage. The Catheter is packaged with the electrode array retracted within the protective, removable orange-colored Catheter tip sheath. Before use, remove the protective orange sheath. Inspect the Catheter for any damage such as broken or crushed areas of the Catheter, sharp or protruding edges at the distal tip, or any excessive bends or kinks in the Catheter shaft. Do not use the Catheter if any damage or irregularity is found. See Figure 4.

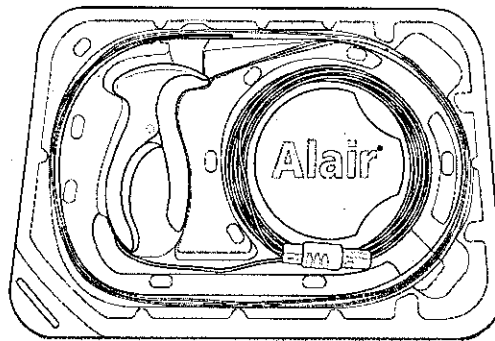


Figure 4: Alair® Catheter in Tray

5. The distal portion of the Catheter shaft has marker bands that are spaced 5mm apart to aid in the positioning of the Catheter electrode array. Do not use the Catheter if the marker bands are missing. See Figure 5.

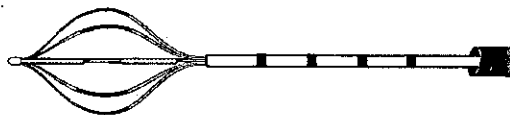


Figure 5: Alair® Catheter with its four Marker Bands, spaced 5mm apart

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6. Hold the Catheter handle in the palm of your hand, with the thumb and forefinger just below the Alair® logo. Then, squeeze the forward handle back towards the back handle, ensuring that the electrode array expands properly. Verify that the electrode array opens fully and evenly. See Figure 6.

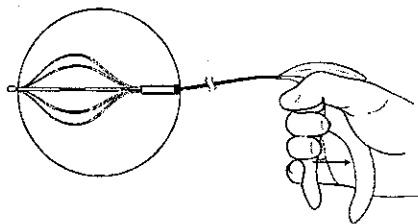


Figure 6: Alair® Catheter Electrode Array Expanded

7. Relax the electrode array by releasing the front handle. See Figure 7. Do not use the Catheter if the electrode array does not expand or relax properly.

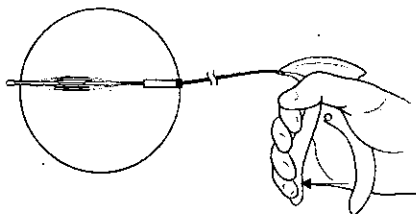


Figure 7: Alair® Catheter Electrode Array Relaxed

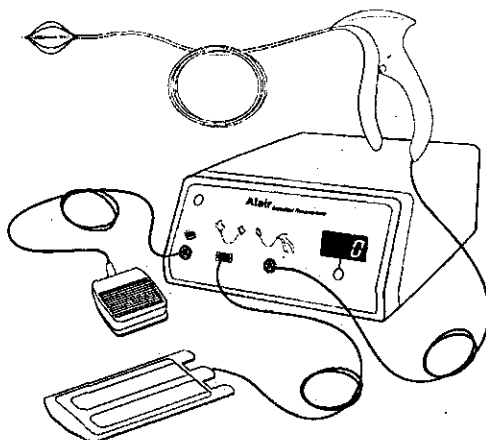


Figure 8: Alair® RF Controller Set-up

Alair® Bronchial Thermoplasty System Set-up and Operation

The Alair® Catheter is intended to be used in conjunction with the Alair® Controller. Please read the Alair® RF Controller Model ATS 200 Operator's Manual before using the Alair System.

Figure 8 illustrates the Alair® RF Controller Model ATS 200 set up.

Consult the Alair® RF Controller Model ATS 200 Operator's Manual for specific instructions on:

- Controller Installation;
- Controller Power-Up;
- Connection of Components and Accessories;
- Controller Modes;
- Periodic Maintenance and Repair;
- Troubleshooting; and
- Technical Specifications.

Patient Preparation

1. Administer prophylactic prednisone or equivalent at a dosage of 50 mg/day for the 3 days before the procedure, the day of the procedure and the day after the procedure to minimize post procedure inflammation.
2. Verify the patient remains a good candidate for bronchoscopy under moderate sedation prior to initiation of the procedure (Mayse et al 2007)⁵. Postpone the procedure if any of the following conditions apply:
 - Prescribed prednisone was not taken on the 3 days before bronchoscopy.
 - SpO₂ is less than 90% on room air.
 - Increase in asthma symptoms in last 48 hours requiring more than 4 puffs/day on average of rescue bronchodilator over pretreatment usage.
 - Asthma exacerbation or changing dose of systemic corticosteroids for asthma (up or down) in the past 14 days.
 - Active respiratory infection, active allergic sinusitis, or other clinical instability.
 - Physician feels for any reason the procedure should be postponed.
3. Prepare the patient for bronchoscopy. Follow patient management protocols according to staffing, training, and individual institution-specific policies and guidelines for bronchoscopy.
4. Place the patient return electrode securely on the patient in accordance with manufacturer's instructions.
5. Introduce the flexible bronchoscope through the nose or mouth as appropriate. See Figure 9 below.

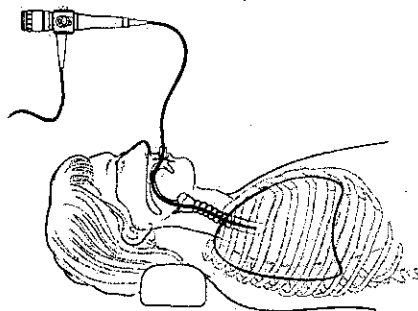


Figure 9: Bronchoscope navigation into patient's airways

6. Navigate the bronchoscope to the targeted site and position the bronchoscope so that the targeted site is in bronchoscopic view.

Alair® Catheter Use

1. Before inserting the catheter into the bronchoscope, ensure the electrode array is relaxed.
2. Advance the catheter into the bronchoscope working channel *being careful not to kink the catheter shaft*. Kinking of the catheter shaft could result in failure of the catheter electrode array to open fully in tortuous anatomy. See PRECAUTIONS.

⁵ Mayse ML, Lavolette M, Rubin AS, Lampron N, Simoff M, Duhamel D, Musani, AI, Yung RC, Mehta AC. Clinical Pearls for Bronchial Thermoplasty. J Bronchol. 2007, 14:115-123.

3. Avoid deflecting the bronchoscope while the electrode array is within the bend of the bronchoscope's working channel as this could result in damage to the Catheter and failure of the Catheter to operate properly. See **PRECAUTIONS**.
4. Advance the Catheter through the bronchoscope until the distal tip of the Catheter shaft is in bronchoscopic view. If the device encounters significant resistance during insertion, do not force it. In especially tortuous anatomy it may be necessary to relax the bronchoscope's deflection mechanism until the device passes smoothly. See **Figure 10** below.

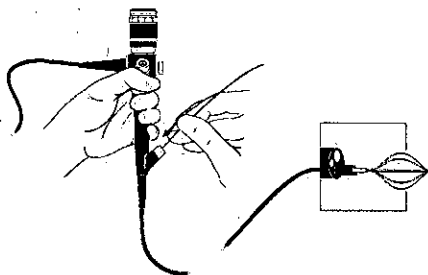


Figure 10: Alair® Catheter introduced through working channel of bronchoscope

5. Advance the Catheter to the targeted site under bronchoscopic vision. Do not advance the Catheter into bronchi in which the Catheter cannot be seen under bronchoscopic vision. Advancing the catheter under such conditions may result in pneumothorax, pneumomediastinum or other harm or injury to the patient. See **WARNINGS**.
6. Do not treat the right middle lobe because of the potential susceptibility of the right middle lobe to transient obstruction as a result of inflammation or edema due to certain anatomical characteristics. The narrow diameter of the lobar bronchus and acute take-off angle may create poor conditions of drainage that may cause patient harm or injury such as atelectasis or difficulty in re-inflation (Right Middle Lobe Syndrome). See **WARNINGS**.
7. Do not reposition the bronchoscope with the Catheter advanced beyond the distal end of the bronchoscope as this may result in harm or injury to the patient. See **WARNINGS**.
8. Once at the targeted site, squeeze the handle together to expand the electrode array partially so that the electrodes are close to or just touching the targeted site.
9. With the electrode array partially expanded, adjust the axial position of the electrodes in the airway to position the active electrodes (exposed 5mm center region of the array electrodes) as desired. Expand the array until all four electrodes firmly contact the airway wall. *Do not over-expand the electrode array* as this may cause one or more of electrodes to deploy inward or 'invert'. If an electrode inverts, relax the electrode array and then re-expand the array in a large, straight airway, confirming proper deployment before returning to the area being treated. In most cases, full expansion of the Catheter electrode array will NOT require the catheter handle to be squeezed completely.
10. Proper contact of the electrodes with the airway wall should be confirmed visually. See **Figure 11** below.

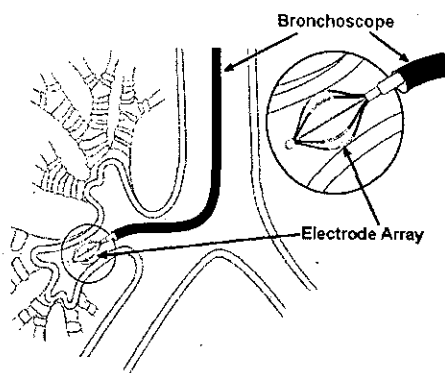


Figure 11: Alair® Catheter in the Airway

11. Before delivering RF energy, make certain that all electrodes are in contact with the airway wall. See **PRECAUTIONS**.
12. Deliver RF energy to the targeted region by pressing and releasing the footswitch once. The Controller will deliver energy automatically according to preset parameters for time, energy, power, and temperature.
13. To manually terminate RF energy delivery, if necessary, press and release the footswitch again.

Note: The Controller will automatically shut off the RF energy if it detects atypical energy delivery or temperature response.

14. The Controller is programmed to alert the user with both audible and visual cues if re-deployment of the electrode array or replacement of the Catheter is required. Please refer to the Alair® RF Controller Model ATS 200 Operator's Manual for more detailed instructions on these audible sounds and light displays.

Note: If RF energy delivery ends prematurely, it may be necessary to re-deploy the electrode array and begin RF energy delivery again. If the problem persists, replace the Catheter.

15. Reposition the Catheter and repeat the steps above making 5mm proximally placed contiguous treatments. The catheter's marker bands are spaced 5mm apart to assist with contiguous placement. See Figure 12.

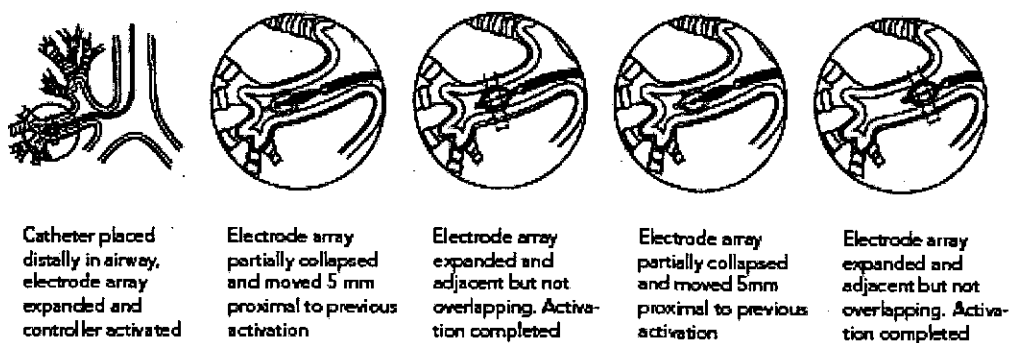


Figure 12: Contiguous Placement and Activation

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16. Once the procedure is complete, relax the Catheter handle to relax the electrode array before removing the Catheter from the bronchoscope or before withdrawing the Catheter into the bronchoscope for airway navigation. To manipulate the bronchoscope with the Catheter in the working channel, withdraw the Catheter approximately 10 cm into the bronchoscope so the electrode array is proximal to the bend in the distal tip of the bronchoscope.
17. Once the treatment is complete, remove the Catheter from the bronchoscope. Disconnect the Catheter from the Controller, and dispose of the used Catheter per your institution's biohazard procedures. Remove the return electrode from the patient. Disconnect the patient return electrode from the Controller, and dispose of the patient return electrode per your institution's biohazard procedures.

Post Procedure Care

1. Follow appropriate institutional guidelines for post procedure care. It is recommended that patients should be carefully monitored and discharged only after they are deemed to be stable and have adequate (comparable to pre-procedure) lung function, mental status, and are able to adequately take liquids.
2. Recommended post procedure assessments are based on the criteria that were used in clinical trials of bronchial thermoplasty (Mayse et al 2007) and include:
 - 2 to 4 hour recovery/monitoring period following each procedure
 - Spirometry, breath sounds, and vital signs (heart rate, blood pressure, temperature, respiratory rate, pulse oximetry) before discharge
 - Discharge if post bronchodilator FEV₁ is within 80% of the pre procedure value and patient is feeling well
 - Verify patient has gag reflex and is able to take liquids
 - Remind patient to take prophylactic prednisone or equivalent the day following bronchoscopy
 - Caution patient about the potential adverse events that they might experience including hemoptysis, fever, cough, and worsening of asthma symptoms. Patients should be advised to consult their physician if they experience any of these adverse events, or asthma symptoms that are not controlled by their reliever medications.
 - Contact patient via phone calls at 1, 2 and 7 days to assess post procedure status
 - Office visit at 2 to 3 weeks to assess clinical stability and schedule subsequent bronchial thermoplasty procedures as appropriate

HOW SUPPLIED

The Alair® Bronchial Thermoplasty System Catheter Model ATS 2-5 is supplied sterile and is for SINGLE USE ONLY. Do not re-sterilize or reuse the Catheter, as this may result in patient harm or injury, transmittal of infectious disease, or product malfunction.

MAINTENANCE AND TROUBLESHOOTING

- If mucus builds up in the airways and obscures visualization, remove the catheter from the bronchoscope, provide irrigation with sterile saline, and suction the resulting fluid from the airways.
- If the electrode array does not expand or relax properly, remove the Catheter from the bronchoscope and squeeze and relax the Catheter handle to visually confirm that the electrode array is functioning properly. If it is not functioning properly, replace the Catheter and continue with the bronchial thermoplasty procedure.
- If you are alerted to auditory or visual cues from the Controller, consult the Alair® Bronchial Thermoplasty RF Controller Model ATS 200 Operator's Manual for operating and troubleshooting guidelines for the Controller.

CUSTOMER SERVICE

All questions or concerns related to the Catheter should be directed to Asthmatx Customer Service or an authorized Asthmatx representative. No product may be returned without prior authorization. Please contact Asthmatx Customer Service or an authorized Asthmatx representative for a Return Material Authorization (RMA) number. See "Contact Us".

PRODUCT WARRANTIES

Asthmatx warrants until the expiration date marked on each Product (the "Warranty Period"), the Alair® Catheter sold hereunder will be free from material defects in materials, function and workmanship and will conform to Asthmatx's specifications in effect as of the date of manufacture. This limited warranty extends only to Customer as original purchaser unless otherwise agreed upon in writing by Asthmatx.

If during the Warranty Period: (i) Asthmatx is notified promptly upon discovery of any defect in the Alair® Catheter (ii) such Alair® Catheter is returned, shipping charges prepaid, to Asthmatx's designated facility with the prior approval of Asthmatx with a valid RMA number, and (iii) Asthmatx's inspections and tests determine that the Alair® Catheter is indeed defective and the Alair® Catheter has not been subjected to any of the conditions set forth below under "Warranty Exclusions," then, as Customer's sole remedy and Asthmatx's sole obligation under the foregoing warranty, Asthmatx will, at Asthmatx's option, replace without charge the defective Alair® Catheter or provide exchange credit. Any Alair® Catheter that has been replaced under this warranty shall have warranty coverage until the expiration date marked on the replacement Alair® Catheter.

WARRANTY EXCLUSIONS

THE WARRANTY SET FORTH IN "PRODUCT WARRANTIES" SHALL NOT APPLY IF THE DEFECTIVE ALAIR® CATHETER (A) HAS BEEN SUBJECTED TO ABUSE, MISUSE, NEGLECT, NEGLIGENCE, ACCIDENT, IMPROPER TESTING, IMPROPER INSTALLATION, IMPROPER STORAGE, IMPROPER HANDLING OR USE CONTRARY TO ANY DOCUMENTATION OR INSTRUCTIONS ISSUED BY ASTHMATX, (B) HAS BEEN REPAIRED OR ALTERED, (C) HAS NOT BEEN INSTALLED, OPERATED, AND MAINTAINED IN ACCORDANCE WITH THE DOCUMENTATION OR OPERATED OUTSIDE OF THE ENVIRONMENTAL SPECIFICATIONS FOR THE ALAIR® CATHETER; (D) HAS FAILED DUE TO AN ACT OF NATURE, INCLUDING BUT NOT LIMITED TO FIRE, FLOOD, TORNADO, EARTHQUAKE, HURRICANE OR LIGHTNING OR (E) HAS BEEN USED WITH ANY

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SYMBOL LEGEND

	Model Number
	Caution: Consult Accompanying Documents
	Radiation sterilized. Sterility guaranteed if package unopened or undamaged.
	Lot Number
	Manufacturer Name
	Use by
	For SINGLE-USE ONLY.
	For sale or use by or on order of a physician only

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Patient Brochure

Alair® Bronchial Thermoplasty System

Cover

This brochure describes a new procedure for treating severe asthma in adults.

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Why doctors use this

You have severe asthma. Your asthma is severe because the asthma drugs you take now do not control your asthma symptoms.

Your doctor wants to use the ALAIR SYSTEM to treat your severe asthma. This treatment is called Bronchial Thermoplasty (BT). BT is not an asthma medicine. Your doctor thinks your health is good enough to have this done.

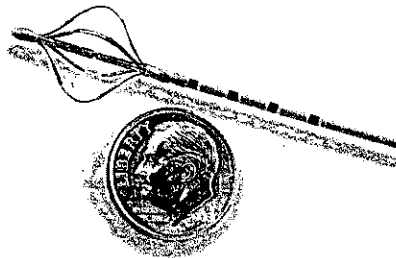
If you decide to have this treatment, you will need to do what your doctor asks you to do or you may be harmed.

What is the ALAIR SYSTEM?

The ALAIR SYSTEM has two main parts:

- A small tube with 4 wires at the end. See Figure 1.

Figure 1: Actual size of tip of ALAIR tube



- A machine that heats the wires.

You need to decide if BT is right for you. You will be treated by a doctor who has been trained and knows how to use it correctly.

What is BT?

BT shrinks the muscles in your airway walls by heating them. This may allow your airways to stay more open and help you breathe better.

Who can have this treatment? (Indication for Use)

The Alair Bronchial Thermoplasty System is indicated for the treatment of severe persistent asthma in patients 18 years and older whose asthma is not well controlled with inhaled corticosteroids and long acting beta agonists.

Who cannot have this treatment? (Contraindications)

You cannot have this treatment if you have:

- **An implant with electronics.** Tell your doctor if you have any implants. BT may keep the implant from working correctly.
- **Problems taking certain drugs.** Tell your doctor if you have ever had a problem taking any kind of drugs. Your doctor will use some drugs to perform BT. Your doctor needs to make sure the drug he or she uses will not hurt you.
- **Have had this treatment before.** Tell your doctor if you have had BT before.
- **You cannot have this treatment if you are less than 18 years old.** No one has tested BT in patients younger than 18 years.

You cannot have this treatment while the following conditions are present:

- **An active respiratory infection.** Tell your doctor if you think you have an infection, fever, or your asthma is worse than usual. If your infection is in your lungs or airway, BT may harm you.
- **Have had an asthma attack or changed your oral corticosteroid dose in the last 2 weeks.** Tell your doctor if either of these happened in the last 2 weeks. If you have had an asthma attack or changed your oral corticosteroid dose in the last 2 weeks, BT may harm you.
- **A blood clotting problem.** Tell your doctor if you take any drugs to keep your blood from clotting. Some call these drugs blood thinners. If you have a blood clotting problem, BT may harm you.

Clinical Study

In 2007, doctors studied nearly 300 patients who had severe asthma. In this study, they saw how well BT worked and what side effects patients had. Doctors treated about 200 people with BT. This was the "BT Group". Doctors treated another group in a similar way, but they did not heat their airways. This was the "Sham Group". Patients did not know which group they were in. Doctors studied these patients for a year after their

last treatment. We do not know how well patients did beyond one year. This is still being studied.

What are the Risks and Side Effects of BT?

Right after their doctors treated them, many patients in the study had side effects. Table 1 shows how many people had each side effect. The table shows side effects that occurred in 1 or more out of every 100 patients, and occurred more often in the BT group.

Table 1: Short Term and Long Term Side Effects

Type of Side Effect	Short-Term Period		Long-Term Period	
	BT Group	Sham Group	BT Group	Sham Group
Related to Breathing	(out of every 100 patients)		(out of every 100 patients)	
More than one symptom of asthma	52	39	27	43
Wheezing	15	6	4	3
Chest pain	14	13	3	1
Shortness of breath	11	6	2	1
Chest discomfort	9	10	2	1
Infection in the lower airways	8	2	3	6
Collapse of part of the lung	5	0	0	0
Swelling of the airways	4	2	7	5
Bleeding [†]	3	0	0	0
Blocked airways	3	0	0	0
Pneumonia	2	0	3	2
Blood in mucus	2	1	1	1
Abnormal breath sounds	2	0	0	0
Intense swelling of airways	1	0	0	0
Infection in the lower airways caused by a virus	1	0	0	0
Narrowing of airways	1	0	0	0
Fluid in lungs	1	0	0	0
Related to Ear, Nose and Throat				
Infection in the upper airways	20	11	30	26
Swelling of the nose and/or throat	5	7	11	5
Infection in the upper airways caused by a virus	4	2	6	7
Acute Sinusitis	3	2	4	8
Rhinitis	2	0	4	6
Swelling of throat	2	1	1	1
Increased mucus in upper airways	1	0	0	0
All Other				
Headaches	14	9	5	3
Fever	4	2	0	1
Influenza	4	2	4	12
Upset stomach	4	2	2	4
Anxiety	4	0	1	2

Type of Side Effect	Short-Term Period		Long-Term Period	
	BT Group	Sham Group	BT Group	Sham Group
Nausea	3	4	1	1
High blood pressure	3	2	3	3
Urinary tract infection	1	1	3	1
Bleeding during the procedure	1	0	0	0

* One instance of bleeding occurred 31 days after a BT treatment and was treated with a medical procedure.

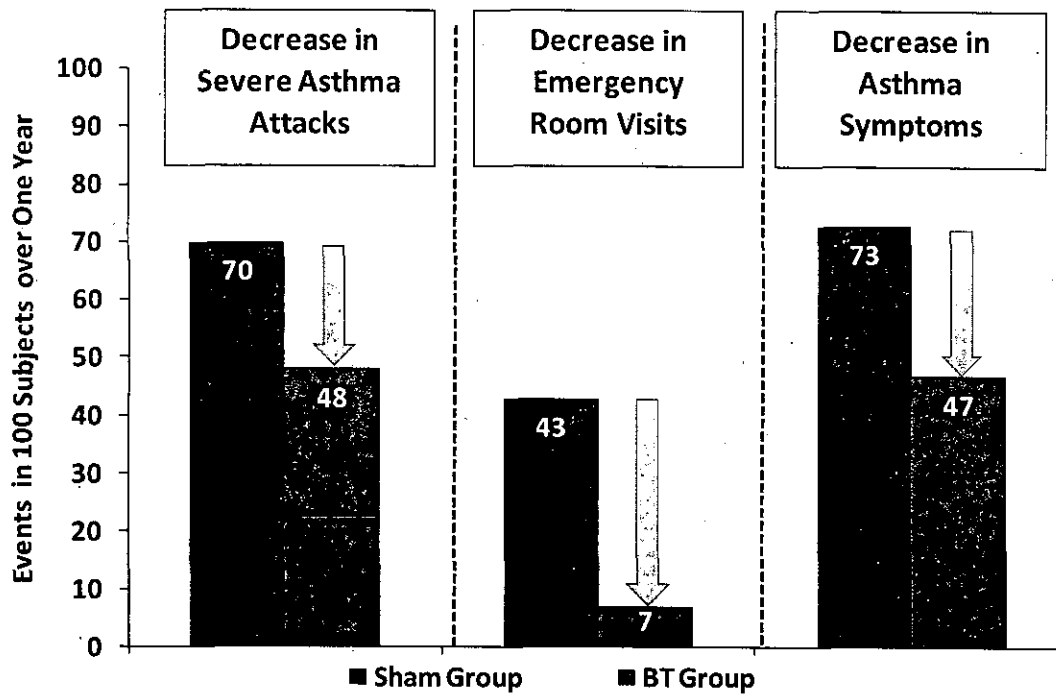
How to read this table:

- Short term: from start of first treatment until 6 weeks after third treatment.
- Long term: from 6 weeks after last treatment until 1 year after last treatment.
- In the table, some patients had more than one side effect.
- Look at Table 1.
 - Think of a group of 100 patients.
 - Look at the column that says "short term".
 - Go down that column to the row that reads "more than one symptom of asthma."
 - This row means that 52 out of every 100 patients had "more than one symptom of asthma" sometime after their first treatment until 6 weeks after their third treatment.
 - On the same row, now look at the "long term" column.
 - You see there were 27 out of every 100 patients who had "more than one symptom of asthma" in the long term period.
 - The 52 and the 27 are not separate groups of patients. Some patients may be counted in both groups:
 - One or more patients who had a "short term" effect may have also had a "long term" effect. Meaning he or she did not get better.
 - One or more patients who did not have a "short term" effect may have had a "long term" effect. Meaning he or she got worse later.
 - One or more patients who had a "short term" effect may not have had a "long term" effect. Meaning their problem went away.
 - We do not know how well patients will do beyond a year after their treatment.

What are the Benefits of BT?

The study showed that the people in the BT Group had fewer severe asthma attacks, visits to the emergency room, and asthma symptoms as shown in Figure 2.

Figure 2: Benefits of BT



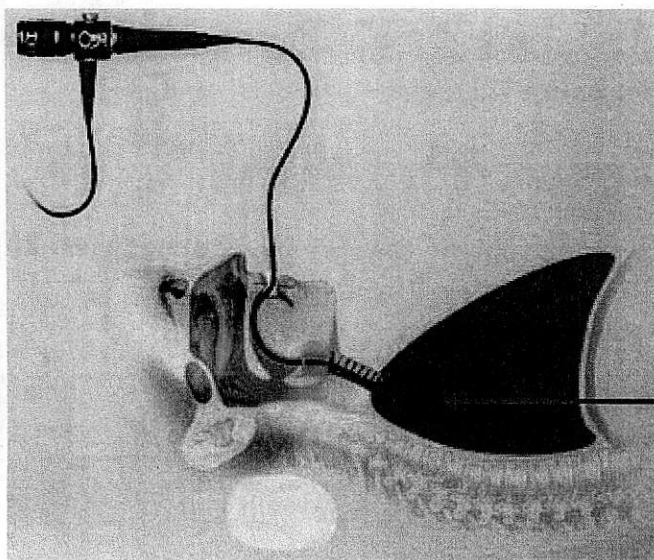
The BT Group also lost on average 3 fewer days per patient from work, school, or other daily activities due to asthma symptoms. This was for one year after treatment compared to the Sham Group. This is not shown in Figure 2.

What will happen if you decide to have the BT treatment for your severe asthma?

- There will be 3 treatments. There will be 3 weeks in between each treatment.
- You will prepare for each treatment by taking a 50-mg steroid pill by mouth once a day for 3 days before the treatment.
- You will also take a 50-mg steroid pill on the day of the treatment.
- On **each** BT treatment day, your doctor will test your lungs. He or she will do this by checking how much air you can blow out.
- Your doctor will make sure you don't have an infection. An infection would delay the treatment.

- Your doctor will tell you what he or she will do during BT.
- Your doctor will:
 1. Give you drugs to make you sleepy.
 2. Put a small tube called a bronchoscope through your mouth into your airways. See Figure 3.

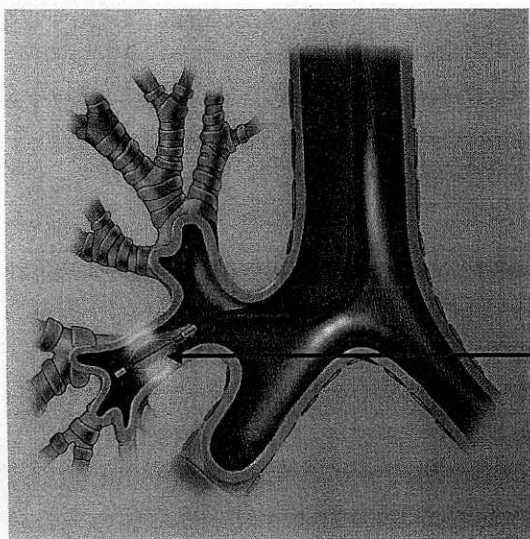
Figure 3: Placement of Bronchoscope into your lungs



Bronchoscope placed through the mouth into the lung

3. Put the smaller ALAIR tube through the bronchoscope. The wires on its end will touch your airways. See Figure 4.

Figure 4: Placement of ALAIR tube in your lungs

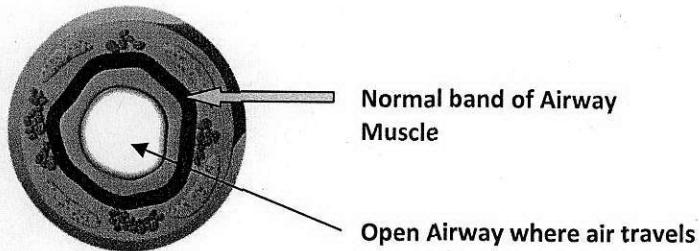


Wires of ALAIR tube opened to contact the inside of your airways

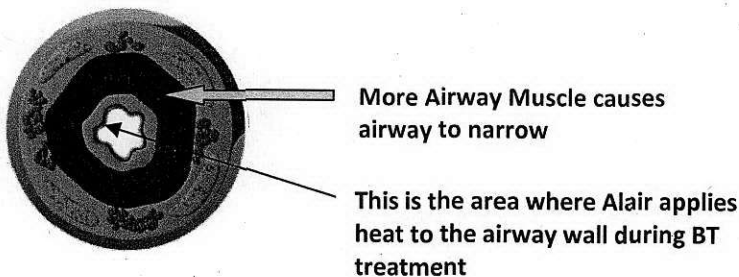
4. Heat the wires on the end of the small ALAIR tube to reduce some of the airway muscle tissue. You won't feel this because your doctor gave you drugs. See Figure 5 for how airways look before and after.

Figure 5: Airways Before and After BT Treatment

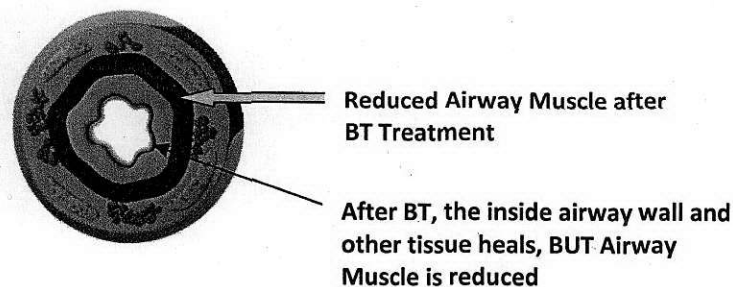
Airway of Person Without Asthma



Airway of Person with Severe Asthma



Airway of Person with Severe Asthma after Treatment



5. Move the small ALAIR tube to more places and treat them the same way.
6. Take the small ALAIR tube and the bronchoscope out.
7. Watch over you as you wake up and recover.

After each BT treatment,

- You have to take 50-mg steroid pill the day after.
- Your doctor will contact you by phone to check on you:
 - the day after your treatment
 - the day after that, and
 - a week after your treatment
- You will still have to take your asthma medicine.

After your airways heal from your first treatment, you will go back to your doctor for your second treatment. Your doctor will treat more of your airways. After you get well from that, your doctor will treat the rest of your airways in your third treatment.

Use your rescue inhaler if your asthma symptoms get bad. Tell your doctor if you needed to use your rescue inhaler.

Where to learn more about the ALAIR SYSTEM and BT:

- Contact your doctor, or
- Call:

Asthmatx, Inc.
888 Ross Drive, Suite 100
Sunnyvale, CA 94089
www.asthmatx.com

Toll Free: 877-810-6060

About Severe Asthma

What happens when you have severe asthma?

Air travels in and out of your lungs through airways, which are tubes. There are tiny muscles in the walls of the airways. People who have severe asthma have larger muscles in their airways than other people. The airways close down when these muscles contract.

What happens when your airways close down?

When airways close down it can be harder to breathe. Your chest may feel tight. You may wheeze or cough. Asthma medicines usually open up the airways. These medicines do not always work well in patients who have severe asthma.

Thank you for considering this new treatment for severe asthma.

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